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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/526,479 | 04/08/2005 | Duncan McGregor | GRT/117-533 | 4224 |

23117 7590 04/24/2009

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| EXAMINER | |
|---|---|
| EPPS SMITH, JANET L | |
| ART UNIT | PAPER NUMBER |
| 1633 | |
| MAIL DATE | DELIVERY MODE |
| 04/24/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/526,479 | MCGREGOR ET AL. | |
| | Examiner | Art Unit | |
| | Janet L. Epps-Smith | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *11-19 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,20-25 and 27-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-44 are presently pending. Claim 11—19 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

2. Claims 1-10, 20-25, and 27-44 are presently pending for examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Response to Arguments*

### *Drawings*

4. The objection to the drawings under 37 CFR 1.83(a) are withdrawn in response to Applicant's submission of new Replacement Sheets.

### *Claim Objections*

5. The objection to claims 5 and 10 is withdrawn in response to Applicant's amendment to the claims.

### *Claim Rejections - 35 USC § 102*

6. Claims 1, 2, 4, 6, 10, 20-24, 27-32, and 34-44 remain rejected under 35 U.S.C. 102(b) as being anticipated by Schatz et al (US Patent 6,156,511) (of record 07/03/07), for the reasons of record.

7. Applicant's arguments filed 8/21/08 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that the Schatz et al. reference does not teach wherein the disclosed methods encodes a protein having

"cis-activity," or further wherein the "encoded protein binds specifically to the DNA molecule from which it is expressed."

8. First, contrary to Applicant's assertions, the instant claims are not limited to only those DNA constructs that encode proteins which bind specifically from the molecule from which it is expressed. The instant claims recite wherein the DNA encoding a peptide "***capable*** of non-covalently binding directly or ***indirectly***.." To the extent that the scope of the claims encompass wherein the peptide *indirectly* binds the DNA target sequence, the claims do not require that the encoded protein or peptide binds specifically to its target sequence.

9. Furthermore, in regards to Applicant's allegations that the constructs of Schatz et al. do not possess cis-activity, Schatz et al. clearly teach methods of making and using a library, wherein the vector includes the DNA domain in which the DNA-binding protein binds to (ie encodes a target sequence). The interaction between the DNA binding protein and DNA is non-covalent, and is affect by such parameters as temperature, pH, ionic strength, etc (column 13, lines 45-65). Furthermore, Schatz teaches:

> "the peptide library is constructed so that the DNA binding protein can bind to the recombinant DNA expression vector that encodes the fusion product of interest. The method of generating the peptide library of the invention comprises the steps of (a) constructing a recombinant DNA vector that encodes a DNA binding protein and contains a binding site for he DNA binding protein; (b) inserting into the coding sequence of the DNA binding protein in the vector of step (a) a coding sequence for a peptide such that the resulting vector encodes a fusion protein comprises the DNA binding protein and the peptide; (c) transforming a host cell with the vector of step (b) and (d) culturing the host cell transformed in step (c) under conditions suitable for expression of the fusion protein (column 2, lines 41-55).

10. Although Schatz et al. describes a specific embodiment that includes the lac repressor operons, which bind the lac repressor proteins, which are fused to a peptide

of interest of the library (see figure 1), this reference also teaches that suitable DNA binding proteins include proteins with known DNA binding domains, such as those with helix-turn-helix, helix-loop-helix and zinc finger proteins (column 7, lines 4-45), and that the protein to be expressed for fusion to the DNA binding domain, the members of the library include antibodies and fragments there of (column 5, lines 23-33; column 22, line 40 - column 23 line 5). He teaches that the vectors expressing the DNA and DNA-binding protein libraries are expressed in host cells such as e coli (which reads on a bacterial transcription/translation environment), and that the peptide library contains at least $10^6$ different members (column 6, lines 47-49; column 11 lines 11).

11. In regards to Applicant's assertions that the lac repressor operon system of Schatz et al. does not teach a plurality of DNA molecules encoding proteins having "cis-activity" according to the embodiments of the claimed invention, Applicants have improperly limited the scope of the disclosure of Schatz et al. Contrary to Applicant's assertions, see for example one particularly embodiment of the Schatz et al. reference which clearly envisions a plurality of DNA vectors encoding proteins having cis-activity for a linker segment within the DNA vector from which it is was encoded:

1. A method of isolating a DNA binding protein comprising:

(a) providing a recombinant DNA vector comprising a coding sequence for a peptide having a specific affinity for a receptor in frame with a DNA segment encoding a linker;

(b) inserting a library of oligonucleotides encoding different potential DNA binding proteins into multiple copies of the recombinant DNA vector in frame with the peptide coding sequence and the linker to form a library of different vectors encoding different fusion proteins, each comprising a potential DNA binding protein, a linker and the peptide, the fusion proteins differing in the potential DNA binding proteins;

(c) transforming host cells with the library of different vectors to form transformed host cells;

(d) culturing the transformed host cells under conditions suitable for expression of the fusion proteins, whereby, if a fusion protein comprises a potential DNA binding protein with affinity for a vector encoding the fusion protein, the fusion protein binds to the vector to form a complex;

(e) lysing the transformed host cells under conditions such that complexes formed in (d) remain associated;

(f) contacting the complexes with a receptor under conditions conducive to specific binding of the peptide to the receptor;

(g) isolating complexes bound to the receptor, the complexes containing vectors encoding DNA binding proteins.

Based upon the description of the above method, particularly wherein it recites "inserting a library of oligonucleotides encoding ***different potential DNA binding proteins into multiple copies*** *of the recombinant DNA vector,"* it is clear that the teachings of Schatz et al. comprises "wherein a plurality of different DNA constructs are expressed together and each expressed peptide is non-covalently linked to the DNA from which it was produced." Therefore contrary to Applicant's allegations it is clear that Schatz et al. teaches the method for producing an *in vitro* peptide expression library according to the claimed invention. Applicant's arguments do not take the place of evidence of non-obviousness.

***Claim Rejections - 35 USC § 103***

12. Claims 3, 5, 7, 8, 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz et al (US Patent 6,156,511) (of record 07/03/07) as applied to claim 1 above, and further in view of Praszkier et al (Role of CIS in Replication of an IncB Plasmid. Journal of Bacteriology, 1999. 181(9):2765-2772 (listed in applicant's IDS dated 5/27/05).

13. Applicant's arguments filed 08/21/2008 have been fully considered but they are not persuasive. Applicants argue that the Schatz et al. reference fails to disclose a method according to claim 1, wherein the DNA construct and encoded protein are selected to have cis-activity," or "teach or suggest a method wherein a plurality of different DNA constructs are expressed together and each expressed peptide is non-covalently linked to the DNA from which it was produced." Applicants allegations have been addressed above, therefore the arguments set forth above in regards to the rejection of claims 1, 2, 4, 6, 10, 20-24, 27-32, and 34-44 under 35 USC 102(b) are incorporated here.

14. Applicants further alleged that the examiner's reasoning for combining the teachings of Praszkier et al. with the teachings of Schatz et al. was based on hindsight and knowledge of the present invention.

15. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

16. Furthermore, contrary to Applicant's assertions, and in the absence of evidence to the contrary, it would have been obvious to the skilled artisan at the time the invention was made to combine the teachings of Schatz et al on a method of making and using a malleable library of various DNA-binding proteins that noncovalently bind to the DNA that encodes them with the teaching of Praskier on the ability of Rep A to directly noncovalently interact with it's CIS and Ori regions, and that the RepA proteins, CIS and Ori regions are highly homologous between well known plasmids, and are capable of exchanging CIS and ORI regions between the plasmids resulting in the maintenance of the RepA proteins of binding to the CIS and Ori region because the RepA DNA binding properties and plasmids encoding them as taught by Praskier were well known in the art at the time of the invention, and that the methods of making and using the library as taught by Schatz were well known in the art at the time of the invention, and all of he claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective function, and the combination would have yielded predictable results to one or ordinary skill in the art at the time of the invention (See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007)).

17. Claim 33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz et al (US Patent 6,156,511) (of record 07/03/07) as applied to claim 1 above, and further in view of Edwards et al (US Patent 5,716,780).

18. Applicant's arguments filed 08/21/2008 have been fully considered but they are not persuasive. Applicants argue that the Schatz et al. reference fails to disclose a method according to claim 1, wherein the DNA construct and encoded protein are selected to have cis-activity," or "teach or suggest a method wherein a plurality of different DNA constructs are expressed together and each expressed peptide is non-covalently linked to the DNA from which it was produced." Applicants allegations have been addressed above, therefore the arguments set forth above in regards to the rejection of claims 1, 2, 4, 6, 10, 20-24, 27-32, and 34-44 under 35 USC 102(b) are incorporated here.

19. Therefore, absent evidence to the contrary, all of the claimed elements were known in the prior art, as being disclosed in Schatz et al. in view of Edwards et al., and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one of ordinary skill in the art at the time of the invention ((See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)).

20. Claim 25 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz et al (US Patent 6,156,511) (of record 07/03/07) as applied to claim 1 above, and Szostak et al (US Patent 6,281,344) further in view of Mattheakis et al (An in vitro

polysome display system for identifying ligands from very large peptide libraries. PNAS, 1994.91:9022-9026) (listed in applicant's IDS dated 05/27/05).

21. Applicant's arguments filed 08/21/2008 have been fully considered but they are not persuasive. Applicants argue that the Schatz et al. reference fails to disclose a method according to claim 1, wherein the DNA construct and encoded protein are selected to have cis-activity," or "teach or suggest a method wherein a plurality of different DNA constructs are expressed together and each expressed peptide is non-covalently linked to the DNA from which it was produced." Applicants allegations have been addressed above, therefore the arguments set forth above in regards to the rejection of claims 1, 2, 4, 6, 10, 20-24, 27-32, and 34-44 under 35 USC 102(b) are incorporated here.

22. Therefore, absent evidence to the contrary, all of the claimed elements were known in the prior art, as being disclosed in Schatz et al. and Szostak et al. in view of Mattheakis et al., and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one of ordinary skill in the art at the time of the invention ((See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)).

***Conclusion***

23. No claims are allowed.

24. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/

Primary Examiner, Art Unit 1633